Claims

1. (Currently amended) A humanized CC49 antibody, comprising:

a light chain complementarity determining region (L-CDR)1, a L-CDR2, and a L-CDR3, a heavy chain complementarity determining region (H-CDR)1, a H-CDR2, and a H-CDR3, all of a parent CC49 antibody, wherein ~~a~~ the L-CDR3 of the humanized CC49 antibody or of ~~a functional~~an antigen binding fragment of the humanized CC49 antibody comprises a non-conservative amino acid substitution[[,]] and ~~wherein the humanized CC49 antibody~~ has a high binding affinity for TAG-72, compared to ~~a~~ the parent CC49 antibody, wherein the parent CC49 antibody is HuCC49V10, deposited as ATCC Accession No. PTA-5416.

2. (Previously Presented) The antibody of claim 1, wherein the non-conservative substitution is a tyrosine to proline substitution.

3. (Previously Presented) The antibody of claim 1, wherein the non-conservative substitution is at position 91.

4. (Previously Presented) The antibody of claim 1, wherein the non-conservative substitution is at a position that corresponds to a ligand contact residue.

5. (Canceled)

6. (Previously Presented) The antibody of claim 1, wherein the L-CDR1 and L-CDR2 are a human antibody L-CDR1 and L-CDR2, respectively.

7. (Canceled)

8. (Previously Presented) The antibody of claim 1, wherein the high binding affinity is at least about 1.2×10^{-8} M.

9. (Canceled)

10. (Previously Presented) The antibody of claim 1, wherein the antibody is minimally immunogenic.

11. (Previously Presented) The antibody of claim 1, wherein the antibody further comprises an effector molecule.

12. (Previously Presented) The antibody of claim 11, wherein the effector molecule is a detectable label.

13–15. (Canceled)

16. (Previously Presented) The antibody of claim 1, further comprising at least one additional non-conservative amino acid substitution in the L-CDR1.

17–19. (Canceled)

20. (Currently amended) A humanized CC49 antibody, ~~wherein a nucleic acid sequence encoding the antibody has an ATCC Accession number comprising~~deposited as ATCC Accession number PTA-4182 or ATCC Accession number PTA-4183.

21. (Withdrawn) A nucleic acid molecule encoding the humanized monoclonal antibody of claim 1.

22. (Withdrawn) A vector comprising the nucleic acid of claim 21.

23. (Currently amended) A humanized CC49 antibody, comprising:

~~a~~ four variable light framework regions and ~~a~~ four variable heavy framework regions of a human antibody;

a light chain complementarity determining region (L-CDR)1, a L-CDR2, a L-CDR3, a heavy chain complementarity determining region (H-CDR)1, a H-CDR2, and a H-

CDR3, wherein at least one complementarity determining region (CDR) is a human antibody CDR and remaining CDRs are murine CC49 antibody CDRs;

a non-conservative substitution of a first residue, wherein the first residue is in the L-CDR3 of the antibody; and

a substitution of a second residue, wherein the second residue is in a any L-CDR or H-CDR of the antibody;

wherein the humanized CC49 antibody has a high binding affinity for TAG-72 and is minimally immunogenic, compared to the parent HuCC49V10 antibody.

24. (Previously Presented) The antibody of claim 23, wherein the non-conservative substitution of the first residue is a tyrosine to proline substitution.

25. (Previously Presented) The antibody of claim 23, wherein the non-conservative substitution of the first residue is at position 91.

26. (Previously Presented) The antibody of claim 25, wherein the non-conservative substitution of the first residue at position 91 is a tyrosine to proline substitution.

27. (Previously Presented) The antibody of claim 23, wherein the antibody further comprises an effector molecule.

28. (Previously Presented) The antibody of claim 27, wherein the effector molecule is a detectable label.

29–31. (Canceled)

32. (Withdrawn) A method of detecting a TAG-72-expressing tumor in a subject, comprising:

contacting a sample from the subject *in vivo* or *in vitro* with the antibody of claim 1 for a sufficient amount of time to form an immune complex; and

detecting the presence of the immune complex, wherein the presence of the immune complex demonstrates the presence of the TAG-72-expressing tumor.

33. (Withdrawn) The method of claim 32, wherein the tumor is a colorectal tumor, a gastric tumor, a pancreatic tumor, a breast tumor, a lung tumor, an adenocarcinoma, or an ovarian tumor.

34. (Withdrawn) The method of claim 32, wherein the antibody further comprises an effector molecule.

35. (Withdrawn) The method of claim 34, wherein the effector molecule is a detectable label or a toxin.

36-43. (Canceled)

44. (Withdrawn) A method of treating a subject having a tumor that expresses TAG-72, comprising administering to the subject a therapeutically effective amount of the antibody of claim 1, wherein administering the therapeutically effective amount of the antibody of claim 1 inhibits the growth of the tumor or reduces the size of the tumor, thereby treating the subject.

45. (Withdrawn) The method of claim 44, wherein the administration of a therapeutically effective amount of the antibody of claim 1 does not elicit a human anti-murine antibody response in a subject.

46. (Canceled)

47. (Withdrawn) The method of claim 44, wherein the antibody further comprises an effector molecule.

48. (Withdrawn) The method of claim 47, wherein the effector molecule is a toxin or a radioactive isotope.

49–51. (Canceled)

52. (Previously Presented) A pharmaceutical composition comprising a therapeutically effective amount of the antibody of claim 1 in a pharmaceutically acceptable carrier.

53–66. (Canceled)

67. (Previously Presented) The antibody of claim 23, wherein the non-conservative substitution of the first residue at position 91 is a tyrosine to proline substitution, the substitution of the second residue at position 27b is a valine to leucine substitution, the L-CDR1, L-CDR2, L-CDR3, H-CDR1, H-CDR2, and H-CDR3 are the parent CC49 antibody L-CDR1, L-CDR2, L-CDR3, H-CDR1, H-CDR2, and H-CDR3, respectively, and the parent CC49 antibody is HuCC49V10.

68. (New) A humanized CC49 antibody, comprising:

a light chain complementarity determining region (L-CDR)1, a L-CDR2, and a L-CDR3, a heavy chain complementarity determining region (H-CDR)1, a H-CDR2, and a H-CDR3, all of a parent CC49 antibody, wherein the L-CDR3 of the humanized CC49 antibody or of an antigen binding fragment of the humanized CC49 antibody comprises a non-conservative amino acid substitution at position 91 and has a high binding affinity for TAG-72, compared to the parent CC49 antibody, wherein the parent CC49 antibody is HuCC49V10.

69. (New) The humanized CC49 antibody of claim 68, wherein the non-conservative substitution is a tyrosine to proline substitution.

70. (New) A humanized CC49 antibody, comprising:

a light chain complementarity determining region (L-CDR)1, a L-CDR2, and a L-CDR3, a heavy chain complementarity determining region (H-CDR)1, a H-CDR2, and a H-CDR3, all of a parent CC49 antibody, wherein the L-CDR3 of the humanized CC49 antibody or of an antigen binding fragment of the humanized CC49 antibody comprises a tyrosine to proline

substitution at position 91 and has a high binding affinity for TAG-72, compared to the parent CC49 antibody, wherein the parent CC49 antibody is HuCC49V10.

71. (New) The antibody of claim 70, wherein the high binding affinity is at least about 1.2×10^{-8} M.

72. (New) The antibody of claim 70, wherein the humanized CC49 antibody is minimally immunogenic.

73. (New) The antibody of claim 70, wherein the humanized CC49 antibody further comprises an effector molecule.

74. (New) The antibody of claim 73, wherein the effector molecule is a detectable label.

75. (New) A pharmaceutical composition comprising a therapeutically effective amount of the antibody of claim 70 in a pharmaceutically acceptable carrier.

76. (New) A method of detecting a TAG-72-expressing tumor in a subject, comprising:

contacting a sample from the subject *in vivo* or *in vitro* with the antibody of claim 70 for a sufficient amount of time to form an immune complex; and

detecting the presence of the immune complex, wherein the presence of the immune complex demonstrates the presence of the TAG-72-expressing tumor.

77. (New) The method of claim 76, wherein the tumor is a colorectal tumor, a gastric tumor, a pancreatic tumor, a breast tumor, a lung tumor, an adenocarcinoma, or an ovarian tumor.

78. (New) The method of claim 76, wherein the antibody further comprises an effector molecule.

79. (New) The method of claim 78, wherein the effector molecule is a detectable label or a toxin.

80. (New) A humanized CC49 antibody, comprising:

four variable light framework regions and four variable heavy framework regions of a human antibody;

a light chain complementarity determining region (L-CDR)1, a L-CDR2, and a L-CDR3 of the parent HuCC49V10 antibody, a heavy chain complementarity determining region (H-CDR)1, a H-CDR2, and a H-CDR3of the parent HuCC49V10 antibody;

a non-conservative substitution of a residue at position 91 in the L-CDR3 of the antibody; and

a substitution of a residue at position 27b of L-CDR1 of the antibody;

wherein the humanized CC49 antibody has a high binding affinity for TAG-72 and is minimally immunogenic, compared to a parent HuCC49V10 antibody.

81. (New) The humanized CC49 antibody of claim 80, wherein the substitution at position 91 is a proline to tyrosine substitution and the substitution at position 27b is a valine to leucine substitution.

82. (New) A humanized CC49 antibody, comprising:

four variable light framework regions and four variable heavy framework regions of a human antibody;

a light chain complementarity determining region (L-CDR)1, a L-CDR2, and a L-CDR3 of the parent HuCC49V10 antibody, a heavy chain complementarity determining region (H-CDR)1, a H-CDR2, and a H-CDR3of the parent HuCC49V10 antibody;

a tyrosine to proline substitution at position 91 in the L-CDR3 of the antibody; and

a valine to leucine substitution at position 27b of L-CDR1 of the antibody;

wherein the humanized CC49 antibody has a high binding affinity for TAG-72 and is minimally immunogenic, compared to a parent HuCC49V10 antibody.

83. (New) The antibody of claim 82, wherein the humanized CC49 antibody further comprises an effector molecule.

84. (New) The antibody of claim 83, wherein the effector molecule is a detectable label.

85. (New) A pharmaceutical composition comprising a therapeutically effective amount of the antibody of claim 82 in a pharmaceutically acceptable carrier.

86. (New) A method of detecting a TAG-72-expressing tumor in a subject, comprising:

contacting a sample from the subject *in vivo* or *in vitro* with the antibody of claim 82 for a sufficient amount of time to form an immune complex; and

detecting the presence of the immune complex, wherein the presence of the immune complex demonstrates the presence of the TAG-72-expressing tumor.

87. (New) The method of claim 86, wherein the tumor is a colorectal tumor, a gastric tumor, a pancreatic tumor, a breast tumor, a lung tumor, an adenocarcinoma, or an ovarian tumor.

88. (New) The method of claim 86, wherein the antibody further comprises an effector molecule.

89. (New) The method of claim 88, wherein the effector molecule is a detectable label or a toxin.